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Characterization and risk factors for aortic dilatation in pediatric patients with bicuspid aortic valve☆

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ABSTRACT

Introduction and objectives: Dilatation of the ascending aorta associated with bicuspid aortic valve is a major cause of morbidity and mortality in adults. The main objective was to recognize the aortic involvement in children, its characteristics and risk factors.
Methods: Aortic measures of all pediatric patients with bicuspid aortic valve followed in a tertiary pediatric hospital between 1997 and 2015 were retrospectively taken. Patients with syndromes associated with aortic dilatation were excluded (n = 17).
Results: Two hundred and six patients were included, 67.9% males. The commonest opening pattern was horizontal: 137 (66.7%). Half of the patients (101) had a history of surgical aortic coarctation, 46 (22.3%) had ≥moderate aortic valve stenosis and 13 (6%) had ≥moderate aortic insufficiency. Mean follow-up time was 6.1 (4.9) years; diagnosis of aortic dilatation was made during the first year of follow-up. Progression of the dilatation of the ascending aorta was noted in 17.1%, and of the aortic root in 2.5%. More than one-third (80/206) had aortic dilatation (*z*-score > 2). The ascending aorta was exclusively affected in 70/80 patients, with sparing of the aortic root. In the multivariate analysis, patients with dilatation of the ascending aorta were associated with absence of coarctation ($p = 0.001$) and vertical opening pattern ($p = 0.007$).
Conclusions: Pediatric patients with bicuspid aortic valve warrant medical follow-up for the frequent association with valve impairment and/or dilatation of the ascending aorta.

Caracterización y factores de riesgo de dilatación aórtica en pacientes pediátricos con válvula aórtica bicúspide

Palabras clave:
Válvula aórtica bicúspide
Dilatación
Aneurisma aórtico
Senos de Valsalva
Pediatría
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RESUMEN

Introducción y objetivos: La dilatación de la aorta ascendente asociada a válvula aórtica bicúspide es una causa mayor de morbimortalidad en adultos. El objetivo principal fue reconocer la afectación aórtica en niños, así como sus características y factores de riesgo.
Métodos: Se realizaron retrospectivamente las mediciones aórticas de todos los pacientes pediátricos con válvula aórtica bicúspide seguidos en un hospital pediátrico terciario entre 1997 y 2015. Se excluyeron los pacientes con síndromes asociados a dilatación aórtica (n = 17).
Resultados: Se incluyeron 206 pacientes, de los cuales el 67,9% eran varones. El patrón de apertura más común fue horizontal: 137 (66,7%). La mitad de los pacientes (101) tenía historia de coartación aórtica, 46 de ellos (22,3%) con estenosis aórtica ≥ moderada y 13 (6%) con insuficiencia aórtica ≥ moderada. El seguimiento medio fue de 6,1 (4,9) años; el diagnóstico de dilatación aórtica se realizó durante el primer

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año de seguimiento. La progresión de la dilatación de la aorta ascendente se documentó en el 17,1%, y en el 2,5% en la raíz aórtica. Más de un tercio (80/206) presentó dilatación aórtica (*z-score* > 2). La afectación exclusiva de la aorta ascendente se produjo en 70/80 pacientes, con preservación de la raíz aórtica. En el análisis multivariado, los pacientes con dilatación de la aorta ascendente se asociaron a ausencia de coartación (p = 0,001) y patrón de apertura vertical (p = 0,007).
Conclusiones: Está justificado el seguimiento en los pacientes pediátricos con válvula aórtica bicúspide debido a la frecuente asociación con disfunción valvular y/o dilatación aórtica.

Introduction

Bicuspid aortic valve is the most prevalent congenital heart disease in adults, affecting between 1 and 2% of the population and being responsible for more deaths and complications than any other congenital heart disease.[1,2] Major complications include valve dysfunction (stenosis and/or regurgitation), as well as dilatation of the aortic root and/or ascending aorta, which can lead to endocarditis and aortic dissection respectively. This is a congenital heart disease, thus in many occasions it is diagnosed during infancy. In addition, even though the inheritance pattern is unknown, familial aggregation has been described[3] and the study of first-degree relatives is nowadays indicated.[4] Therefore, the finding of bicuspid aortic valve in asymptomatic pediatric patients is relatively common. Progressive dilation of the aortic root and/or the ascending aorta in patients with bicuspid aortic valve is variable, ranging from 26 to 84%.[5,6] The ascending aorta is dilated in adults when exceeds 40 mm or 27.5 mm/m^2 in patients of short stature.[7] In children the aortic measure is adjusted for body surface area[8] and compared with the published data[9,10]; it is considered dilated when the *z*-score is greater than +2 standard deviations. Some risk factors for progression of aortic dilatation have been proposed both for adults[11] and for children,[12] but are inconsistent. In the pediatric population, the prevalence, risk factors and indications for treatment of patients with bicuspid aortic valve and aortic dilatation is unknown. Although there are no published case reports of aortic dissection in pediatric patients, they have been described in adults and its incidence is higher than in the general population.[6,13,14] Identifying patients at higher risk for complications associated with bicuspid aortic valve during the pediatric age could prevent the emergence of serious events in adulthood. The main objective of this study was to recognize the aortic involvement in children with bicuspid aortic valve, its characteristics and risk factors.

Methodology

All patients with bicuspid aortic valve followed in our unit between 1997 and 2015 were identified. Patients with known diseases associated with aortic dilatation were excluded: Marfan syndrome (3/17), Loeys–Dietz syndrome (1/17), Turner syndrome (2/17), 22q11.2 deletion (4/17), and 7 with congenital heart disease: transposition of great arteries (1/17), tetralogy of Fallot (1/17), pulmonic stenosis with ventricular septal defect (2/17), pulmonary agenesis (2/17) and aortopulmonary window (1/17). Finally, a total of 206 patients were selected for the study. The Ethical Committee of the Hospital approved the study, and informed consent was waived.

Aortic measures were taken following the recommendations of the American Society of Echocardiography.[15] Briefly, two-dimensional parasternal long axis view was used at the time of maximum expansion (mid-systole). The aortic root was measured at the level of the sinus of Valsalva and the ascending aorta was measured distal to the sinotubular junction as it crosses in front of the right pulmonary artery (see online data supplement). Two observers (LSS and ASR) corroborated the valve-opening pattern and made all the measurements in the first and last echocardiography available on the server (General Electrics EchoPack). Complete data was available in all but 2 patients for the sinus of Valsalva measurements, and all but 1 patient for the ascending aorta measurements.

Valve opening pattern was classified according to the presence or absence of a raphe (see Fig. 1). Patients with left to noncoronary raphe were classified as vertical pattern together with right to noncoronary raphe because of low numbers. Aortic stenosis was defined when more or equal to moderate (mean echocardiographic gradient equal or above 20 mmHg). Aortic insufficiency was defined when more or equal to moderate (taking into account vena contracta, jet width, pressure half time and reversal aortic flow in thoracic descending aorta).

Measurements of the aortic root and ascending aorta were adjusted to body surface area and compared to normalized published data.[10] Aortic dilatation was defined when the *z*-score was higher than +2 standard deviations. It was classified as mild if the *z*-score was between +2 and +4 standard deviations, moderate if the *z*-score was between +4 and +6 and severe if the *z*-score was higher than +6.[12] Progression was defined as change of category at follow-up.

Location of aortic dilatation was classified according to Verma et al[16]: type 1 involvement of both the aortic root and ascending aorta, type 2 exclusive involvement of the ascending aorta, type 3 exclusive involvement of the aortic root.

Continuous variables are presented as mean (SD) or median and IQR, depending on the normality of their distribution. Nominal and ordinal variables are summarized as frequencies and percentages. Patient characteristics according to the location of aortic dilatation were compared using Chi-square test, *F* Fisher's test or two sample *t* tests, as appropriate. Progression of aortic root and ascending aorta dilatation was analyzed using non-parametric test of related samples. Stepwise multiple linear regression was used to assess the association between aortic size (of the sinuses of Valsalva and the ascending aorta) and various risk factors. Splines were used for age at diagnosis and age at last visit because of non-linear relationship with sinus of Valsalva and ascending aorta *z*-scores. Logistic regression was used to assess the risk factors for aortic dilatation (*z*-score $\geq$ 2). A two-tailed *p* value <0.05 was considered statistically significant. We were unable to perform multivariate analysis for dilation of sinus of Valsalva (*z*-score $\geq$ 2) because of insufficient number of events.

Results

Table 1 summarizes demographic variables and associated heart disease of the 206 patients included in the study, compared according to the location of aortic dilatation.